

## REMARKS

### **A. Status of the Claims**

Claims 1, 6-12, 15, and 18-26 were pending at the time of the action. Claims 2-5, 13, 14, 16, 17, and 27-46 were previously canceled. No claims have been amended or added. Therefore, claims 1, 6-12, 15, and 18-26 are currently pending and presented for reconsideration.

### **B. Anticipation Rejection**

Claims 1, 6, 9, 11, and 12 are rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by Sharon (U.S. Patent 5,789,208). Applicants respectfully traverse.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP § 2131. Sharon fails to teach at least three of the elements of the current claims and therefore cannot anticipate the present claims.

Sharon fails to teach a method that expresses “antibodies or antibody fragments on the surface of said plurality of yeast host cells,” as required by the current claims. Rather, Sharon appears to teach expression of the recombinant product on a *phage* surface, which is outside the scope of the present claims. Sharon, col. 13, lines 47-51; col. 24, lines 23-25; col. 29, lines 36-39. In particular, Sharon teaches that antibodies are displayed on the surface of phage by fusing the antibody to a phage coat protein. Sharon, col. 24, lines 23-25. No where does Sharon teach a method that displays or expresses antibodies on the surface of *yeast* host cells and none of the Examples teach such a method. Therefore, Sharon does not teach a method where yeast host cells express antibodies or antibody fragments on their surface.

Sharon also fails to teach a method that includes selecting a yeast host cell that expresses a desired antibody or antibody fragment on its surface. At best, Sharon suggests the possibility

that a method for screening of surface display libraries might be developed in the future that could be used to screen antibody libraries created by the disclosed methods. However, Sharon does not enable a person of skill in the art to perform such a surface display screening method. Rather, as discussed in detail above, the only surface display expression taught by Sharon is the expression of the antibody library on the surface of a phage. Therefore, Sharon fails to teach a method that includes a step of selecting a yeast host cell that expresses a desired antibody or antibody fragment on its surface.

Finally, with respect to claims 6 and 9, Sharon fails to teach a method where a yeast host cell that expresses an antibody on the cell surface is contacted with an antigen. Rather, Sharon teaches a method where a cell population capable of producing antibodies is introduced to an antigen. Sharon, col. 10, lines 62-64. A person having skill in the art would recognize that the cell population in the method taught by Sharon does not produce the antibody and display it on the cell surface prior to introducing the cell to the antigen. *See Sharon, col. 10, line 62 to col. 11, line 16* (“Antibody ***producing*** cells are removed from an animal, or cell culture, and exposed to antigen. The ***antigen-stimulated cells*** can be used . . . to generate a population of ***antibody producing*** hybridomas.” (emphasis added)). Rather, it would be clear to a person having skill in the art that exposing the cell to the antigen stimulates the cell to produce the antibody. In contrast, the currently claimed method involves contacting a yeast host cell that ***already displays*** an antibody on its surface with an antigen. As Sharon does not teach a method where a yeast host cell that expresses an antibody on the cell surface is contacted with an antigen, it cannot anticipate the current claims.

For at least these reasons, the rejection is improper and withdrawal thereof is respectfully requested.

### C. Obviousness Rejection

Claims 7, 8, 10, 15, 18, 19, and 20-26 are rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Sharon in view of one of Yokoyama (U.S. Patent 5,646,011), Slamon (U.S. Patent 4,918,162), or Civin (U.S. Patent 5,081,030).

The cited references, alone or in combination, fail to teach or suggest each element of the claims. The failure of an asserted combination to teach or suggest each and every feature of a claim remains fatal to an obviousness rejection under 35 U.S.C. § 103. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974) (emphasis added) (to establish *prima facie* obviousness of a claimed invention, all the claim features must be taught or suggested by the prior art); MPEP § 2143.03. As the Supreme Court stated in *KSR Int'l v. Teleflex Inc.*, “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). Thus, it remains well-settled law that obviousness requires at least a suggestion of all of the features in a claim. *See In re Wada and Murphy, citing CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

All of the claims rejected as obvious ultimately depend from independent claim 1. If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. MPEP § 2143.03. None of the cited references, alone or in combination, teach or suggest all the elements of current claim 1. As discussed in detail above, at a minimum, Sharon fails to provide a teaching or suggestion of expressing antibodies or antibody fragments on the surface of yeast host cells, selecting a yeast host cell that expresses a desired antibody or antibody fragment on its surface, and contacting a yeast host cell that expresses an antibody on the cell surface with an antigen. Yokoyama, Slamon, and Civin also fail to provide a teaching or

suggestion of any of these elements and, in fact, it is not asserted that they do in the Action. Yokoyama is cited for allegedly teaching the step of labeling the antigen with a fluorescent label. Slamon has been cited for allegedly teaching the step of releasing a selected antibody from the surface of the outer membrane. Finally, Civin has been cited for allegedly teaching cell separation techniques. As none of the cited references, alone or in combination, teach or suggest all the elements of the current claims, the rejections are improper.

Furthermore, it is important “to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements” in the manner claimed. *KSR Int’l Co. v. Teleflex, Inc.*, 550 U.S. 398, 418 (2007). In particular, the Court noted that there should be an “explicit” analysis regarding “whether there was an **apparent reason** to combine the known elements **in the fashion claimed** by the patent at issue.” *Id.* at 417 (emphasis added).

A person having skill in the art would have no apparent reason to modify or combine the teachings of the cited references to arrive at the currently claimed invention. As discussed above, Sharon appears to teach expression of the recombinant product on a **phage** surface, which is outside the scope of the present claims. Sharon, col. 13, lines 47-51; col. 24, lines 23-25; col. 29, lines 36-39. Sharon specifically teaches that the antibodies are displayed on the surface of phage by fusing the antibody to a phage coat protein. Sharon, col. 24, lines 23-25. No where does Sharon teach a method that expresses antibodies on the surface of **yeast** host cells. Rather, Sharon only teaches methods by which antibodies are displayed on phage. In fact, in its entire disclosure, Sharon mentions yeast cells only twice.

Upon consideration of Sharon, a person having skill in the art would have no reasonable expectation of success in expressing an antibody on the surface of a yeast host cell and in further using such a cell in a surface display screening method to select a yeast host cell expressing a

desired antibody or antibody fragment. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *See Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991); MPEP § 2143.02. None of Yokoyama, Slamon, or Civin are asserted to or in fact remedy the failure of Sharon to teach or suggest expression of antibodies on the surface of yeast host cells, or the use of such yeast cells in a surface display screening method.

For at least these reasons, the rejection should be withdrawn.

**D. Conclusion**

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. The examiner is invited to contact the undersigned attorney with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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